

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Application No.	: 10/625,989	Confirmation No.:	1706
Applicants	: Kenneth SETCHELL, et al.		
Filed	: July 24, 2003		
TC/A.U.	: 1616		
Examiner	: Alton N. PRYOR		
Docket No.	: 3515-104		
Customer No.	: 6449		

**RULE 132 DECLARATION OF RICHARD L. JACKSON**

I, Richard L. Jackson, declare as follows:

1. I am President and CEO of Ausio Pharmaceuticals, LLC, Licensee of the subject patent application.
  
2. My education and experience, which are further detailed in the copy of my resume that is attached hereto as Exhibit A, are as follows. I received a B.S. degree in chemistry in 1963 and a Ph.D. degree in microbiology in 1967, both from the University of Illinois. In addition to my current position as President and CEO of Ausio Pharmaceuticals, LLC, I have held Senior Executive positions in various pharmaceutical companies since the mid-1980's. I also have held numerous academic positions, including fellowships, associate professorships, and full professorships. Furthermore, I have established research centers at the University of Cincinnati College of Medicine and at Baylor College of Medicine, and I have received various honors and awards over the course of my professional career. I also have authored or co-authored hundreds of publications, I am a named inventor on 10 issued patents, and I have served or currently serve on approximately two dozen National Advisory Committees and Boards of Directors.

3. I am familiar with the subject patent application, including the currently pending claims. I am also familiar with the reference cited in the November 18, 2008 Final Office Action, by Alvira, et al.
4. I understand that the claims currently pending in this application recite various compositions relating to enantiomeric equol, particularly the R-enantiomer (R-equol).
5. In my capacity at Ausio Pharmaceuticals, I directed that a pharmacological screening study be undertaken to evaluate and directly compare the biological activities of R-equol, S-equol, and racemic equol in a collection of biochemical assays. Specifically, each of R-equol, S-equol, and racemic equol was screened against a broad spectrum of receptor systems using standard radioligand binding assay methods adapted from the scientific literature. The study was conducted by an outside party, with no interest in the present application, hired by Ausio specifically for the purpose of conducting the study. Attached hereto are descriptions of the study and the results obtained for each of S-Equol (AUS-131—Exhibit B), R-Equol (AUS-132—Exhibit C), and Racemic Equol (AUS-133—Exhibit D). As indicated, reference standards were run as an integral part of each assay to ensure the validity of the results obtained. Percent inhibition results of the complete, broad spectrum of assays are reported.
6. I have reviewed the results of the study and, in my opinion, the results contain several examples of properties unexpectedly possessed by the enantiomeric forms of equol that are not possessed by the racemic mixture. Moreover, the overall results reveal that a commonly held position, namely that only one of the two enantiomers in a known active racemic

mixture is presumed active, is not universally applicable with respect to equol. As the data reveal, in some systems, the S-enantiomer is active while the R- is not. In others, the R-enantiomer is active while the S- is not. In some systems, both enantiomers and the racemate are active, and in one particular system, discussed more fully below, both the S- and R-enantiomers are similarly active, but the racemate is inactive. It is also seen that there is variability in activity between related receptor types.

7. The table below summarizes some of the more significant individual results obtained in the broad spectrum of studies, as referred to above.

**In vitro Pharmacological Screening**

Target	Percent Inhibition (at 10 uM)			Interpretation (re: higher values)
	S-Equol	R-Equol	Racemate	
ER $\alpha$	92	93	94	Positive control
ER $\beta$	98	94	98	Positive control
src Protein Tyrosine Kinase LCK	27	26	1	Oncology indication
Transcription Response Factor, NF-AT	5	32	19	Anti-inflammatory indication, potential MOA
G Protein-coupled Receptor 103	58	14	38	Bone sparing, satiety, CNS effects, inflammation
Monoamine Transporter	16	51	49	CNS, antidepressant
NE Transporter	57	37	50	Antidepressant
Dopamine Transporter	84	88	92	Anti-Parkinsonism

As is clear from the table, the approach of simply resolving a racemate into its separate enantiomers, determining which of the two isomers is the active form (and which is the inactive form), and consequently choosing to prepare a composition using the active form, would not appear to be effective with respect to equol. In my opinion, one could not reliably predict biological activity of the equol enantiomers when armed only with teachings concerning the racemic mixture.

8. The src Protein Tyrosine Kinase (LCK) data provides a clearly surprising and unexpected result. LCK is an important receptor kinase that regulates the growth of cells. When mutated, uncontrolled growth occurs. The studies here have shown that both S- and R-equol inhibit this activity approximately equally (27% and 26% respectively at 10  $\mu$ M concentration). However, racemic equol, which of course contains both R- and S-equol, surprisingly does not inhibit the activity (1% inhibition at the same 10  $\mu$ M concentration). This is a completely unexpected finding. Based on these results, therefore, racemic equol would likely be ineffective in inhibiting cancer growth, for example, but a composition containing the R-enantiomer, as claimed herein, would surprisingly be expected to show potential benefits.

9. The results obtained in the study referred to herein are surprising and would not be expected to be achieved based on the teachings in the reference noted in the November 18, 2008 Final Office Action (Alvira, et al.), or the teachings in the other references of record. Specifically, one could not assume enantiomeric equol compositions would be biologically active or otherwise useful based merely on teachings concerning racemic equol.

U.S. Application No. 10/625,989  
Rule 132 Declaration of Richard L. Jackson

10. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Signed: Richard L. Jackson  
Richard L. Jackson, Ph.D.  
President and CEO  
Ausio Pharmaceuticals, LLC

Date: 6/30/09

1624500.1

## **RICHARD L. JACKSON, PhD**

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### **CURRENT POSITION**

**Auslo Pharmaceuticals, LLC**  
**President and CEO**  
**1776 Mentor Ave.**  
**Cincinnati, OH 45212**  
**513.731.0333**  
**Richard@auslopharma.com**

A specialty pharmaceutical start-up company focused on the development of various medicines. The Company's first drug product is AUS-131 which was licensed from Cincinnati Children's Hospital and Sanitarium, an Australian health food company. The compound currently is being developed as an oral drug. A topical formulation also is being developed. The first clinical studies will begin in Q1, 2008.

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### **PREVIOUS POSITIONS**

**ENTREPRENEUR-IN-RESIDENCE, Cincinnati Children's Hospital** 2003 - 2006

Provided pharmaceutical and commercial input into the Computational Medicine Center proposal; a \$28 million grant was awarded to Cincinnati Children's Hospital from the State of Ohio (Third Frontier Award).

Provided input for the Tomorrow Fund, a Third Frontier award to establish a seed fund at Children's Hospital.

Provided pharmaceutical and drug development expertise for the development of technologies from Children's Hospital. Several technologies were licensed to pharmaceutical companies. Auslo Pharmaceuticals, LLC, Baxion Pharmaceuticals, LLC and Atabios Therapeutics are companies that have been spun-out from these efforts.

**EMERGEN, INC., Salt Lake City, UT**

March 2002 – April 2003

**President and CEO**  
**Chairman, Board of Directors**

In-licensed leuprolgel from Abis Laboratories for the treatment of endometriosis. The research focus was the genetic basis of endometriosis and polycystic ovary syndrome. Identified novel targets for invasive cancers by understanding placental biology.

**ATRIX LABORATORIES, INC., Fort Collins, CO**

November 1, 1998 - 2002

**Senior Vice President, Research and Development**  
**Reported to Mr. D.R. Bethune (CEO & Chairman)**  
**Member of Board of Directors**

Responsible for preclinical, clinical, regulatory, and quality activities for new therapies in dermatology, pain management, and oncology. Five products reached the market place.

**WYETH-AYERST, the Pharma Division of American Home Products**

1993 - 1998

**Senior Vice President, Discovery Research**  
**Reported to Dr. R.I. Levy (President, Wyeth-Ayerst Research)**  
**Deceased**

Responsible for the discovery of innovative, new therapies for Women's Health, Neurological Disorders, Cardiovascular and Metabolic Diseases, Infectious Diseases, Oncology and Immunoinflammatory Diseases. Provided strategic, scientific and administrative leadership for

**Exhibit A**

the worldwide research efforts. Responsible for 1100 people with an annual internal operating budget of \$180 million plus external University and Biotech alliances of \$52 million. Seven products reached the market place.

**MARION MERRELL DOW RESEARCH INSTITUTE**

1985 - 1992

Senior Vice President Discovery Research

Reported to Dr. A. Sjoerdsma/Dr. W. Lovenberg (Presidents - MMD Research Institute)

Responsible for the discovery of drugs for Allergy, Pulmonary Diseases, CNS Disorders, Oncology, Cardiovascular/Metabolic Diseases and Immuno-Inflammatory Diseases. Responsibility for the US discovery operation (350 scientists) with close working relationships with Center Directors in Strasbourg, France, and Milano, Italy.

**UNIVERSITY OF CINCINNATI COLLEGE OF MEDICINE**

1978 - 1984

Head, Division of Lipoprotein Research

Professor, Department of Pharmacology and Cell Biophysics, Biological Chemistry and Medicine

Department Chairman: Dr. A. Schwartz

Established a research center of excellence in cardiovascular diseases.

**BAYLOR COLLEGE OF MEDICINE**

1971 - 1977

Associate Professor, Departments of Medicine and Cell Biology

Department Chairman: Dr. A.M. Gotto, Dr. B. O'Malley

Established a cardiovascular center for research, patient care and education.

**NIH, LABORATORY CHEMICAL PATHOLOGY, NIAMD**

1970 - 1971

Senior Staff Fellow

**NIH, EXPERIMENTAL THERAPEUTICS, NHLBI**

1969 - 1970

Junior Staff Fellow

**BROOKHAVEN NATIONAL LABORATORY**

1967 - 1968

Postdoctoral Fellowship

**PROFESSORSHIPS**

**HADASSAH UNIVERSITY HOSPITAL**, Jerusalem, Israel (November - December, 1974)

**STATE UNIVERSITY OF UTRECHT**, Utrecht, the Netherlands (January - July, 1978)  
Biochemical Laboratory

**INSTITUTO VENEZOLANO DE INVESTIGACIONES CIENTIFICAS**, Caracas, Venezuela  
(October, 1982)

**NATIONAL CARDIOVASCULAR CENTER RESEARCH INSTITUTE**, Osaka, Japan (June - August, 1984)

**ROCKEFELLER UNIVERSITY**, New York (January - July, 1985)

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**EDUCATION**

PhD University of Illinois, Department of Microbiology 1967

BS University of Illinois, Department of Chemistry, 1963

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**HONORS/  
AWARDS**

1969	American Cancer Society Postdoctoral Fellowship
1972	American Heart Association Established Investigator
1974	American Heart Association Lewis Katz Award
1981	The 1000 Contemporary Scientist Most Cited 1965 - 1978
1984	Naio Foundation Award - National Cardiovascular Research Institute, Osaka, Japan

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**NATIONAL  
ADVISORY  
COMMITTEES/  
BOARD OF  
DIRECTORS**

1979 - 1983	NIH Metabolism Study Section
1977 - 1981	American Heart Association Pathology Research Review
1981	American Heart Association Katz Award Committee
1980 - 1982	American Heart Association Program Committee
1982 - 1988	Editorial Board, Journal of Lipid Research
1988 - 1992	Associate Editor, Journal of Lipid Research
1990 - 1992	American Heart Association, Executive Committee at Large
1991 - 1992	University of Cincinnati Cardiovascular Center, Advisory Board
1992 - 1997	Editorial Board, Current Drugs in Research
1992 - 1995	Arthritis Foundation, Scientific Advisory Board
1994 - 1998	American Heart Association, Long-Term Planning Committee
1995 - 1998	Rider University, Scientific Advisory Board
1996 - 1998	Immunex Corporation, Member Board of Directors
1997 - 2000	Princeton University, Chemistry Department Advisory Board
1998 - 2000	ZymoGenetics, Scientific Advisory Board
1999 - 2002	Atrix Laboratories, Member Board of Directors
2001 - 2007	Inflazyme, Member Board of Directors
2002 - 2003	EmerGen, Inc., Member Board of Directors
2003 - Present	Oncothyreon (Biomira), Member Board of Directors
2003 - 2005	MDS Capital, Scientific Advisory Board
2005	AB Biopharma, Member Board of Directors
2006 - Present	Baxion Pharmaceuticals, Chairman, Board of Directors
2006 - Present	Viron Therapeutics, Chairman, Board of Directors
2007 - Present	Leukemia and Lymphoma Society, Member Board for Translational Research

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**PUBLICATIONS**

274 Reviewed Articles  
Over 500 Abstracts and Presentations

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**PATENTS**

10 Issued Patents

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**SpectrumScreen  
Data Report  
Ausio Pharmaceuticals LLC**

Study Completed: August 27, 2007

Report Printed: August 27, 2007

**MDSPS PT#: 1094967**

**Alt. Code 1: Batch: A313-10-5**

**Alt. Code 2:**

**Alt. Code 3:**

**Sample(s): AUS-131**

**M.W.: 242.27**

**Objectives:**

To evaluate, in SpectrumScreen, the activity of test compound AUS-131 (PT# 1094967).



**Pharma Services**

PT# 1094967  
CODE: AUS-131

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## MDS Pharma Services Pharmacology Data Report On Compound AUS-131 For Ausio Pharmaceuticals LLC

Work Order Number: 1-1028408-1      Services Being Reported: SpectrumScreen  
Alternative Work Order No:  
Purchase Order Number:      Total # of Assays: 159  
Compound Information:  
    Compound Code: AUS-131  
    Alternative Code 1: Batch: A313-10-5  
    Alternative Code 2:  
    Alternative Code 3:  
    MDSPS Internal #: 1094967  
    Molecular Weight: 242.27  
Sponsor: Ausio Pharmaceuticals LLC  
    1776 Mentor Avenue  
    Suite 340  
    Cincinnati, OH 45212  
    USA  
Undertaken at: MDS Pharma Services - Taiwan Ltd.  
    Pharmacology Laboratories  
    158 Li-Teh Road, Peitou  
    Taipei, Taiwan 112  
    Taiwan  
Date of Study: August 13, 2007 - August 27, 2007  
Study Directors: Kun-Yuan Lin, MDS Pharma Services - Taiwan Ltd.  
    Kuo-Hsin Chen, MDS Pharma Services - Taiwan Ltd.  
Distribution: Ausio Pharmaceuticals LLC

"This study was conducted according to the procedures described in this report. All data presented are authentic, accurate and correct to the best of our knowledge."

*Kun-Yuan Lin*

Kun-Yuan Lin  
Study Director for Animal Assays

*Kuo-Hsin Chen*

Kuo-Hsin Chen  
Study Director for Biochemical Assays

*Jiann-Wu Wei*

Jiann-Wu Wei, Ph.D.  
Quality Control and Data Reviewer

*Peter Chiu*

Peter Chiu, Ph.D.  
Technical Director

PT #: 1094867  
CODE: AUS-131

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## SUMMARY

### STUDY OBJECTIVE

To evaluate, in Radioligand Binding assays, the activity of compound AUS-131 (PT# 1094967).

### METHODS

Methods employed in this study have been adapted from the scientific literature to maximize reliability and reproducibility. Reference standards were run as an integral part of each assay to ensure the validity of the results obtained. Assays were performed under conditions described in the accompanying "Methods" section of this report. The literature reference(s) for each assay are in the "Literature References" section. If either of these sections were not originally requested with the accompanying report, please contact us at the number below for a printout of either of these report sections.

Where presented,  $IC_{50}$  values were determined by a non-linear, least squares regression analysis using Data Analysis Toolbox™ (MDL Information Systems, San Leandro, CA, USA). Where inhibition constants ( $K_i$ ) are presented, the  $K_i$  values were calculated using the equation of Cheng and Prusoff (Cheng, Y., Prusoff, W.H., *Biochem. Pharmacol.* 22:3099-3108, 1973) using the observed  $IC_{50}$  of the tested compound, the concentration of radioligand employed in the assay, and the historical values for the  $K_D$  of the ligand (obtained experimentally at MDS Pharma Services). Where presented, the Hill coefficient ( $n_H$ ), defining the slope of the competitive binding curve, was calculated using Data Analysis Toolbox™. Hill coefficients significantly different than 1.0, may suggest that the binding displacement does not follow the laws of mass action with a single binding site. Where  $IC_{50}$ ,  $K_i$  and/or  $n_H$  data are presented without Standard Error of the Mean (SEM), data are insufficient to be quantitative, and the values presented ( $K_i$ ,  $IC_{50}$ ,  $n_H$ ) should be interpreted with caution.

### RESULTS

A summary of results meeting the significance criteria is presented in the following sections. Complete results are presented under the section labeled "Experimental Results". Individual responses, if requested, are presented in the appendix to this report.

### SUMMARY/CONCLUSION

Significant results are displayed in the following table(s) in rank order of potency for estimated  $IC_{50}$  and/or  $K_i$  values.

## SUMMARY OF SIGNIFICANT PRIMARY RESULTS

Biochemical assay results are presented as the percent inhibition of specific binding or activity throughout the report. All other results are expressed in terms of that assay's quantitation method (see Methods section).

- For primary assays, only the lowest concentration with a significant response judged by the assays' criteria, is shown in this summary.
- Where applicable, either the secondary assay results with the lowest dose/concentration meeting the significance criteria or, if inactive, the highest dose/concentration that did not meet the significance criteria is shown.
- Unless otherwise requested, primary screening in duplicate with quantitative data (e.g.,  $IC_{50} \pm SEM$ ,  $K_i \pm SEM$  and  $nH$ ) are shown where applicable for individual requested assays. In screening packages, primary screening in duplicate with semi-quantitative data (e.g., estimated  $IC_{50}$ ,  $K_i$  and  $nH$ ) are shown where applicable (concentration range of 4 log units); available secondary functional assays are carried out (30  $\mu M$ ) and MEC or MIC determined only if active in primary assays >50% at 1 log unit below initial test concentration.
- Please see Experimental Results section for details of all responses.

Significant responses ( $\geq 50\%$  inhibition or stimulation for Biochemical assays) were noted in the primary assays listed below:

PRIMARY TESTS							
CAT. #	PRIMARY BIOCHEMICAL ASSAY	SPECIES	CONC.	% INH.	$IC_{50}$ *	$K_i$	$nH$
204410	Transporter, Norepinephrine (NET)	hum	10 $\mu M$	57			
220320	Transporter, Dopamine (DAT)	hum	10 $\mu M$	84			
226010	Estrogen ER $\alpha$	hum	10 $\mu M$	92			
226050	Estrogen ER $\beta$	hum	10 $\mu M$	98			
226300	G Protein-Coupled Receptor GPR103	hum	10 $\mu M$	68			

‡ Partially soluble in *in vitro* test solvent.

\* A standard error of the mean is presented where results are based on multiple, independent determinations.  
gp=guinea pig; ham=hamster; hum=human

## EXPERIMENTAL RESULTS - BIOCHEMICAL ASSAYS

Cat. #	TARGET	BATCH*	SPP.	n=	CONC.	↑% INHIBITION					IC <sub>50</sub>	K <sub>i</sub>	n <sub>H</sub>	R
						%	-100	-50	0	50	100			
200510	Adenosine A <sub>1</sub>	203049	hum	2	10 μM	-6								
200610	Adenosine A <sub>2A</sub>	203053	hum	2	10 μM	22								
200720	Adenosine A <sub>2B</sub>	203104	hum	2	10 μM	9								
203100	Adrenergic α <sub>1A</sub>	203043	rat	2	10 μM	0								
203200	Adrenergic α <sub>1B</sub>	203044	rat	2	10 μM	6								
203400	Adrenergic α <sub>2</sub>	203045	hum	2	10 μM	14								
203820	Adrenergic α <sub>2A</sub>	203046	hum	2	10 μM	-3								
203800	Adrenergic α <sub>2C</sub>	203048	hum	2	10 μM	-2								
204010	Adrenergic β <sub>1</sub>	203050	hum	2	10 μM	-2								
204110	Adrenergic β <sub>2</sub>	203051	hum	2	10 μM	8								
204200	Adrenergic β <sub>3</sub>	203052	hum	2	10 μM	-3								
204480	Adrenomedullin AM <sub>1</sub>	203480	hum	2	10 μM	0								
204470	Adrenomedullin AM <sub>2</sub>	203481	hum	2	10 μM	9								
204600	Aldosterone	203107	rat	2	10 μM	9								
205000	Anaphylatoxin C5a	203237	hum	2	10 μM	1								
205010	Androgen (Testosterone) AR	203102	rat	2	10 μM	5								
210020	Angiotensin AT <sub>1</sub>	203406	hum	2	10 μM	8								
210110	Angiotensin AT <sub>2</sub>	203095	hum	2	10 μM	3								
210700	ANP	203462	hum	2	10 μM	12								
211000	Atrial Natriuretic Factor (ANF)	203189	gp	2	10 μM	-3								
211600	Bombesin BB1	203463	hum	2	10 μM	9								
211700	Bombesin BB2	203464	hum	2	10 μM	1								
211800	Bombesin BB3	203465	hum	2	10 μM	-7								
212510	Bradykinin B <sub>1</sub>	203086	hum	2	10 μM	8								
212610	Bradykinin B <sub>2</sub>	203087	hum	2	10 μM	9								
213610	Calcitonin	203238	hum	2	10 μM	1								
214010	Calcitonin Gene-Related Peptide CGRP <sub>1</sub>	203239	hum	2	10 μM	-13								
214510	Calcium Channel L-Type, Benzothiazepine	203056	rat	2	10 μM	-8								
214600	Calcium Channel L-Type, Dihydropyridine	203057	rat	2	10 μM	5								
215000	Calcium Channel L-Type, Phenyltolylamine	203058	rat	2	10 μM	34								

\* Batch: Represents compounds tested concurrently in the same assay(s). ‡ Partially soluble in *in vitro* test solvent.

† Denotes item meeting criteria for significance

‡ Results with ≥ 50% stimulation or inhibition are highlighted. (Negative values correspond to stimulation of binding or enzyme activity)

R=Additional Comments

gp=guinea pig; ham=hamster; hum=human

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CODE: AUS-231

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## EXPERIMENTAL RESULTS - BIOCHEMICAL ASSAYS

Cat. #	TARGET	BATCH*	SPP.	n=	CONC.	↑% INHIBITION					IC <sub>50</sub>	K <sub>i</sub>	D <sub>50</sub>	R
						%	-100	-50	0	50	100			
216000	Calcium Channel N-Type	203178	rat	2	10 µM	0								
217020	Cannabinoid CB <sub>1</sub>	203177	hum	2	10 µM	9								
217100	Cannabinoid CB <sub>2</sub>	203178	hum	2	10 µM	-8								
244600	Chemokine CXCR1	203471	hum	2	10 µM	5								
218010	Cholecystokinin CCK <sub>1</sub> (CCK <sub>A</sub> )	203408	hum	2	10 µM	13								
218120	Cholecystokinin CCK <sub>2</sub> (CCK <sub>B</sub> )	203488	hum	2	10 µM	8								
219100	Colchicine	203000	rat	2	10 µM	15								
219150	Corticotropin Releasing Factor CRF <sub>1</sub>	203409	hum	2	10 µM	-2								
219500	Dopamine D <sub>1</sub>	202982	hum	2	10 µM	8								
219700	Dopamine D <sub>2</sub>	202984	hum	2	10 µM	-1								
219800	Dopamine D <sub>3</sub>	202985	hum	2	10 µM	3								
219900	Dopamine D <sub>4</sub>	202986	hum	2	10 µM	18								
220200	Dopamine D <sub>5</sub>	202989	hum	2	10 µM	5								
224010	Endothelin ET <sub>A</sub>	203091	hum	2	10 µM	-6								
224110	Endothelin ET <sub>B</sub>	203092	hum	2	10 µM	12								
225510	Epidermal Growth Factor (EGF)	203187	hum	2	10 µM	3								
225800	Erythropoietin EPOR	203487	hum	2	10 µM	6								
♦ 226010	Estradiol ERα	202976	hum	2	10 µM	92								
♦ 226050	Estradiol ERβ	202977	hum	2	10 µM	88								
♦ 226300	G Protein-Coupled Receptor GPR103	202993	hum	2	10 µM	58								
226230	G Protein-Coupled Receptor GPR8	203470	hum	2	10 µM	-4								
226810	GABA <sub>A</sub> Chloride Channel, TBOB	203101	rat	2	10 µM	0								
226600	GABA <sub>A</sub> , Flunitrazepam, Central	203081	rat	2	10 µM	12								
226500	GABA <sub>A</sub> , Muscimol, Central	203080	rat	2	10 µM	-4								
226810	GABA <sub>A</sub>	203158	hum	2	10 µM	-20								
226710	GABA <sub>A</sub>	203159	hum	2	10 µM	-8								
230000	Gabapentin	203001	rat	2	10 µM	0								
231510	Galanthin GAL1	203165	hum	2	10 µM	-1								
231600	Galanthin GAL2	203166	hum	2	10 µM	-4								
232600	Glutamate, AMPA	203157	rat	2	10 µM	-19								

\* Batch: Represents compounds tested concurrently in the same assay(s). ‡ Partially soluble in *in vitro* test solvent.

♦ Denotes item meeting criteria for significance

† Results with ≥ 50% stimulation or inhibition are highlighted. (Negative values correspond to stimulation of binding or enzyme activity)

R=Additional Comments

gp=guinea pig; ham=hamster; hum=human

## EXPERIMENTAL RESULTS - BIOCHEMICAL ASSAYS

Cat. #	TARGET	BATCH*	SPP.	no	CONC.	↑% INHIBITION					IC <sub>50</sub>	K <sub>i</sub>	n <sub>H</sub>	R
						%	-100	-50	0	50	100			
232700	Glutamate, Kainate	203063	rat	2	10 µM	10								
232810	Glutamate, NMDA, Agonism	203064	rat	2	10 µM	-1								
232910	Glutamate, NMDA, Glycine	203065	rat	2	10 µM	0								
233000	Glutamate, NMDA, Phencyclidine	203066	rat	2	10 µM	-8								
234000	Glutamate, NMDA, Polyamine	203067	rat	2	10 µM	-5								
236000	Glycine, Strychnine-Sensitive	203068	rat	2	10 µM	3								
236300	Growth Hormone Secretagogue (GHS, Ghrelin)	203243	hum	2	10 µM	6								
236610	Histamine H <sub>1</sub>	202670	hum	2	10 µM	8								
236710	Histamine H <sub>2</sub>	203069	hum	2	10 µM	8								
236810	Histamine H <sub>3</sub>	202672	hum	2	10 µM	-9								
236900	Histamine H <sub>4</sub>	202673	hum	2	10 µM	-4								
241000	Imidazoline I <sub>2</sub> , Central	202674	rat	2	10 µM	-9								
242500	Inositol Triphosphate IP <sub>3</sub>	203244	rat	2	10 µM	10								
243000	Insulin	203206	rat	2	10 µM	-3								
250400	Leptin	203317	mouse	2	10 µM	-8								
250510	Leukotriene, BLT (LTB <sub>4</sub> )	204039	hum	2	10 µM	9								
250480	Leukotriene, Cysteinyl CysLT <sub>1</sub>	203089	hum	2	10 µM	-1								
250480	Leukotriene, Cysteinyl CysLT <sub>2</sub>	203090	hum	2	10 µM	-21								
251100	Melanocortin MC <sub>1</sub>	203411	hum	2	10 µM	6								
251300	Melanocortin MC <sub>2</sub>	203412	hum	2	10 µM	-3								
251350	Melanocortin MC <sub>3</sub>	203413	hum	2	10 µM	1								
251400	Melanocortin MC <sub>4</sub>	203414	hum	2	10 µM	18								
251600	Melatonin MT <sub>1</sub>	203140	hum	2	10 µM	5								
251700	Melatonin MT <sub>2</sub>	203142	hum	2	10 µM	41								
252200	Motilin	203472	hum	2	10 µM	8								
252610	Muscarinic M <sub>1</sub>	202657	hum	2	10 µM	-3								
252710	Muscarinic M <sub>2</sub>	202658	hum	2	10 µM	0								
252810	Muscarinic M <sub>3</sub>	202659	hum	2	10 µM	1								
252910	Muscarinic M <sub>4</sub>	202660	hum	2	10 µM	0								
253010	Muscarinic M <sub>5</sub>	202661	hum	2	10 µM	-1								
226100	N-Formyl Peptide Receptor FPR1	203240	hum	2	10 µM	-5								

\* Batch: Represents compounds tested concurrently in the same assay(s). ‡ Partially soluble in *in vitro* test solvent.

• Denotes item meeting criteria for significance

† Results with ≥ 50% stimulation or inhibition are highlighted. (Negative values correspond to stimulation of binding or enzyme activity)

R=Additional Comments

gp=guinea pig; ham=hamster; hum=human



## EXPERIMENTAL RESULTS - BIOCHEMICAL ASSAYS

Cat. #	TARGET	BATCH*	SPR	n=	CONC.	†% INHIBITION					IC <sub>50</sub>	K <sub>i</sub>	n <sub>H</sub>	R
						%	-100	-50	0	50	100			
228200	N-Formyl Peptide Receptor-Like FRL1	203241	hum	2	10 µM	-10								
258100	Neuremedin U NMA <sub>1</sub>	203473	hum	2	10 µM	2								
258200	Neuremedin U NMA <sub>2</sub>	203474	hum	2	10 µM	5								
257010	Neuropeptide Y Y <sub>1</sub>	203088	hum	2	10 µM	-10								
257110	Neuropeptide Y Y <sub>2</sub>	203084	hum	2	10 µM	4								
258010	Neurotensin NT <sub>1</sub>	203318	hum	2	10 µM	-3								
258580	Nicotinic Acetylcholine	202888	hum	2	10 µM	-1								
258700	Nicotinic Acetylcholine α1, Bugarotoxin	202981	hum	2	10 µM	10								
258830	Nicotinic Acetylcholine α7, Bugarotoxin	202980	rat	2	10 µM	-5								
260110	Opiate δ (OP1, DOP)	203070	hum	2	10 µM	8								
260210	Opiate κ (OP2, KOP)	203072	hum	2	10 µM	12								
260410	Opiate μ (OP3, MOP)	203074	hum	2	10 µM	-5								
260600	Orphanin ORL <sub>1</sub>	203478	hum	2	10 µM	2								
264500	Phorbol Ester	203078	mouse	2	10 µM	1								
265010	Platelet Activating Factor (PAF)	203007	hum	2	10 µM	8								
265200	Platelet-Derived Growth Factor (PDGF)	202979	mouse	2	10 µM	9								
265500	Potassium Channel [K <sub>v</sub> ]	203079	rat	2	10 µM	3								
265600	Potassium Channel [K <sub>cs</sub> ]	203078	ham	2	10 µM	9								
265800	Potassium Channel [SK <sub>Ca</sub> ]	203002	rat	2	10 µM	4								
265900	Potassium Channel HERG	202994	hum	2	10 µM	9								
268020	Progesterone PR-B	202882	hum	2	10 µM	15								
268030	Prostanoid CRTH2	203352	hum	2	10 µM	18								
268050	Prostanoid DP	202895	hum	2	10 µM	30								
268200	Prostanoid EP <sub>1</sub>	202898	hum	2	10 µM	17								
268410	Prostanoid EP <sub>4</sub>	202897	hum	2	10 µM	5								
268510	Prostanoid, Thromboxane A <sub>2</sub> (TP)	203004	hum	2	10 µM	4								
268700	Purinergic P <sub>2u</sub>	202882	rabbit	2	10 µM	-12								
268810	Purinergic P <sub>2v</sub>	202883	rat	2	10 µM	5								
268500	Retinoid X Receptor RXRα	203477	hum	2	10 µM	0								

\* Batch: Represents compounds tested concurrently in the same assay(s). ‡ Partially soluble in *in vitro* test solvent.

• Denotes item meeting criteria for significance

† Results with ≥ 50% stimulation or inhibition are highlighted. (Negative values correspond to stimulation of binding or enzyme activity)

R=Additional Comments

gp=guinea pig; ham=hamster; hum=human

PT# 1004507  
CODE ABB-131

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## EXPERIMENTAL RESULTS - BIOCHEMICAL ASSAYS

Cat. #	TARGET	BATCH*	SPP.	n=	CONC.	1% INHIBITION					IC <sub>50</sub>	K <sub>i</sub>	n <sub>H</sub>	R
						%	-100	-50	0	50	100			
270000	Rolipram	203130	rat	2	10 µM	0								
270300	Ryanodine RyR3	203478	rat	2	10 µM	7								
271110	Serotonin (5-Hydroxytryptamine) 5-HT <sub>1A</sub>	203108	hum	2	10 µM	-3								
271200	Serotonin (5-Hydroxytryptamine) 5-HT <sub>1B</sub>	203109	rat	2	10 µM	22								
271700	Serotonin (5-Hydroxytryptamine) 5-HT <sub>2B</sub>	203251	hum	2	10 µM	17								
271800	Serotonin (5-Hydroxytryptamine) 5-HT <sub>2C</sub>	203273	hum	2	10 µM	15								
271910	Serotonin (5-Hydroxytryptamine) 5-HT <sub>1</sub>	203164	hum	2	10 µM	-11								
272000	Serotonin (5-Hydroxytryptamine) 5-HT <sub>2</sub>	203174	gp	2	10 µM	4								
272100	Serotonin (5-Hydroxytryptamine) 5-HT <sub>2A</sub>	203003	hum	2	10 µM	9								
272200	Serotonin (5-Hydroxytryptamine) 5-HT <sub>2</sub>	203254	hum	2	10 µM	11								
278110	Sigma σ <sub>1</sub>	203082	hum	2	10 µM	18								
278200	Sigma σ <sub>2</sub>	203083	rat	2	10 µM	15								
279510	Sodium Channel, Site 2	203084	rat	2	10 µM	2								
282510	Somatostatin sst1	203181	hum	2	10 µM	14								
282700	Somatostatin sst2	203182	hum	2	10 µM	3								
282830	Somatostatin sst3	203183	hum	2	10 µM	-1								
282900	Somatostatin sst4	203184	hum	2	10 µM	8								
283000	Somatostatin sst5	203185	hum	2	10 µM	-5								
285510	Tachykinin NK <sub>1</sub>	203180	hum	2	10 µM	-2								
285560	Tachykinin NK <sub>2</sub>	203181	hum	2	10 µM	25								
285710	Tachykinin NK <sub>3</sub>	203182	hum	2	10 µM	-5								
285900	Thyroid Hormone	203171	rat	2	10 µM	-7								
288000	Thyrotropin Releasing Hormone (TRH)	203259	rat	2	10 µM	6								
288200	Transforming Growth Factor-β (TGF-β)	202880	mouse	2	10 µM	11								
202000	Transporter, Adenosine	203088	gp	2	10 µM	6								
218000	Transporter, Choline	203105	rat	2	10 µM	10								

\* Batch: Represents compounds tested concurrently in the same assay(s). ‡ Partially soluble in *in vitro* test solvent.

• Denotes item meeting criteria for significance

† Results with ≥ 50% stimulation or inhibition are highlighted. (Negative values correspond to stimulation of binding or enzyme activity)

R=Additional Comments

gp=guinea pig; ham=hamster; hum=human

File: 1894367  
 CODE: AUB-131

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## EXPERIMENTAL RESULTS - BIOCHEMICAL ASSAYS

Cat. #	TARGET	BATCH*	SPC.	n	CONC.	↑% INHIBITION					IC <sub>50</sub>	K <sub>i</sub>	pH	R
						%	-100	-50	0	50	100			
♦ 220320	Transporter, Dopamine (DAT)	203188	hum	2	10 µM	84								
228400	Transporter, GABA	203059	rat	2	10 µM	5								
252010	Transporter, Monoamine	203179	rabbit	2	10 µM	16								
♦ 204410	Transporter, Norepinephrine (NET)	203581	hum	2	10 µM	57								
274030	Transporter, Serotonin (5-Hydroxytryptamine) (SERT)	203055	hum	2	10 µM	11								
288700	Urotensin II	203234	hum	2	10 µM	-14								
286810	Vanilloid	203133	rat	2	10 µM	-6								
286900	Vascular Endothelial Growth Factor (VEGF)	203598	hum	2	10 µM	28								
287010	Vasoactive Intestinal Peptide VIP <sub>1</sub>	203260	hum	2	10 µM	0								
287520	Vasopressin V <sub>1A</sub>	203097	hum	2	10 µM	2								
287560	Vasopressin V <sub>1B</sub>	203098	hum	2	10 µM	-1								
287810	Vasopressin V <sub>2</sub>	203099	hum	2	10 µM	-20								
288000	Vitamin D <sub>3</sub>	203096	hum	2	10 µM	-8								

\* Batch: Represents compounds tested concurrently in the same assay(s). ‡ Partially soluble in *in vitro* test solvent.

♦ Denotes item meeting criteria for significance

† Results with ≥ 50% stimulation or inhibition are highlighted. (Negative values correspond to stimulation of binding or enzyme activity)

R=Additional Comments

gp=guinea pig; ham=hamster; hum=human

FTV: 1094987  
CODE: ADS-131

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## EXPERIMENTAL RESULTS - BIOCHEMICAL ASSAYS

MDS has an exclusive, worldwide limited use license from Synaptic Pharmaceutical Corporation to perform these assays: Adrenergic Alpha 1D, Adrenergic Alpha 2B, and Dopamine D5 for safety and selectivity profiling. MDS' license excludes performing those assays in connection with drug discovery or development activities where the principal therapeutic mechanism of action of the test compound involves selective binding to a licensed receptor. Customers may contact Synaptic directly if they believe they need a broader license.

**SpectrumScreen  
Data Report  
Ausio Pharmaceuticals LLC**

Study Completed: August 27, 2007

Report Printed: August 27, 2007

**MDSPS PT#: 1094968**

**Alt. Code 1: Batch: A313-84-1**

**Alt. Code 2:**

**Alt. Code 3:**

**Sample(s): AUS-132**

**M.W.: 242.27**

**Objectives:**

To evaluate, in SpectrumScreen, the activity of test compound AUS-132 (PT# 1094968).



**Pharma Services**

PTN: 100-068  
CODE: AUS-132

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## MDS Pharma Services Pharmacology Data Report On Compound AUS-132 For Ausio Pharmaceuticals LLC

Work Order Number: 1-1028406-1

Services Being Reported: SpectrumScreen

Alternative Work Order No:

Purchase Order Number:

Total # of Assays: 150

Compound Information:

Compound Code: AUS-132  
Alternative Code 1: Batch: A313-84-1  
Alternative Code 2:  
Alternative Code 3:  
MDSPS Internal #: 1094558  
Molecular Weight: 242.27

Sponsor: Ausio Pharmaceuticals LLC  
1776 Mentor Avenue  
Suite 340  
Cincinnati, OH 45212  
USA

Undertaken at: MDS Pharma Services - Taiwan Ltd.  
Pharmacology Laboratories  
158 Li-Teh Road, Peitou  
Taipei, Taiwan 112  
Taiwan

Date of Study: August 13, 2007 - August 27, 2007

Study Directors: Kun-Yuan Lin, MDS Pharma Services - Taiwan Ltd.  
Kuo-Hsin Chen, MDS Pharma Services - Taiwan Ltd.

Distribution: Ausio Pharmaceuticals LLC

"This study was conducted according to the procedures described in this report. All data presented are authentic, accurate and correct to the best of our knowledge."




Kun-Yuan Lin  
Study Director for Animal Assays



Kuo-Hsin Chen  
Study Director for Biochemical Assays



Jian-Wu Wei, Ph.D.  
Quality Control and Data Reviewer



Peter Chiu, Ph.D.  
Technical Director

FT # 100000  
CODE: AUS-132

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## SUMMARY

### STUDY OBJECTIVE

To evaluate, in Radioligand Binding assays, the activity of compound AUS-132 (PT# 1094968).

### METHODS

Methods employed in this study have been adapted from the scientific literature to maximize reliability and reproducibility. Reference standards were run as an integral part of each assay to ensure the validity of the results obtained. Assays were performed under conditions described in the accompanying "Methods" section of this report. The literature reference(s) for each assay are in the "Literature References" section. If either of these sections were not originally requested with the accompanying report, please contact us at the number below for a printout of either of these report sections.

Where presented,  $IC_{50}$  values were determined by a non-linear, least squares regression analysis using Data Analysis Toolbox™ (MDL Information Systems, San Leandro, CA, USA). Where inhibition constants ( $K_i$ ) are presented, the  $K_i$  values were calculated using the equation of Cheng and Prusoff (Cheng, Y., Prusoff, W.H., Biochem. Pharmacol. 22:3099-3108, 1973) using the observed  $IC_{50}$  of the tested compound, the concentration of radioligand employed in the assay, and the historical values for the  $K_D$  of the ligand (obtained experimentally at MDS Pharma Services). Where presented, the Hill coefficient ( $n_H$ ), defining the slope of the competitive binding curve, was calculated using Data Analysis Toolbox™. Hill coefficients significantly different than 1.0, may suggest that the binding displacement does not follow the laws of mass action with a single binding site. Where  $IC_{50}$ ,  $K_i$ , and/or  $n_H$  data are presented without Standard Error of the Mean (SEM), data are insufficient to be quantitative, and the values presented ( $K_i$ ,  $IC_{50}$ ,  $n_H$ ) should be interpreted with caution.

### RESULTS

A summary of results meeting the significance criteria is presented in the following sections. Complete results are presented under the section labeled "Experimental Results". Individual responses, if requested, are presented in the appendix to this report.

### SUMMARY/CONCLUSION

Significant results are displayed in the following table(s) in rank order of potency for estimated  $IC_{50}$  and/or  $K_i$  values.



## SUMMARY OF SIGNIFICANT PRIMARY RESULTS

Biochemical assay results are presented as the percent inhibition of specific binding or activity throughout the report. All other results are expressed in terms of that assay's quantitation method (see Methods section).

- For primary assays, only the lowest concentration with a significant response judged by the assays' criteria, is shown in this summary.
- Where applicable, either the secondary assay results with the lowest dose/concentration meeting the significance criteria or, if inactive, the highest dose/concentration that did not meet the significance criteria is shown.
- Unless otherwise requested, primary screening in duplicate with quantitative data (e.g.,  $IC_{50} \pm SEM$ ,  $K_i \pm SEM$  and  $nH$ ) are shown where applicable for individual requested assays. In screening packages, primary screening in duplicate with semi-quantitative data (e.g., estimated  $IC_{50}$ ,  $K_i$  and  $nH$ ) are shown where applicable (concentration range of 4 log units); available secondary functional assays are carried out (30  $\mu M$ ) and MEC or MIC determined only if active in primary assays >50% at 1 log unit below initial test concentration.
- Please see Experimental Results section for details of all responses.

Significant responses ( $\geq 50\%$  inhibition or stimulation for Biochemical assays) were noted in the primary assays listed below:

PRIMARY TESTS							
PRIMARY							
CAT. #	BIOCHEMICAL ASSAY	SPECIES	CONC.	% INH.	$IC_{50}$ *	$K_i$	$nH$
220320	Transporter, Dopamine (DAT)	hum	10 $\mu M$	88			
228010	Estrogen ER $\alpha$	hum	10 $\mu M$	93			
228050	Estrogen ER $\beta$	hum	10 $\mu M$	94			
252010	Transporter, Monoamine	rebbil	10 $\mu M$	51			

‡ Partially soluble in *in vitro* test solvent.

\* A standard error of the mean is presented where results are based on multiple, independent determinations.  
gp=guinea pig; ham=hamster; hum=human

## EXPERIMENTAL RESULTS - BIOCHEMICAL ASSAYS

Cat. #	TARGET	BATCH*	SPP.	n	CONC.	↑% INHIBITION						IC <sub>50</sub>	K <sub>i</sub>	n <sub>H</sub>	R
						%	-100	-50	0	50	100				
200510	Adenosine A <sub>1</sub>	203049	hum	2	10 µM	-4									
200610	Adenosine A <sub>2A</sub>	203053	hum	2	10 µM	33									
200720	Adenosine A <sub>3</sub>	203104	hum	2	10 µM	10									
203100	Adrenergic α <sub>1A</sub>	203043	rat	2	10 µM	13									
203200	Adrenergic α <sub>1B</sub>	203044	rat	2	10 µM	5									
203400	Adrenergic α <sub>1C</sub>	203045	hum	2	10 µM	8									
203620	Adrenergic α <sub>2A</sub>	203046	hum	2	10 µM	5									
203800	Adrenergic α <sub>2C</sub>	203048	hum	2	10 µM	3									
204010	Adrenergic β <sub>1</sub>	203050	hum	2	10 µM	15									
204110	Adrenergic β <sub>2</sub>	203051	hum	2	10 µM	20									
204200	Adrenergic β <sub>3</sub>	203052	hum	2	10 µM	-1									
204480	Adrenomedullin AM <sub>1</sub>	203480	hum	2	10 µM	-11									
204470	Adrenomedullin AM <sub>2</sub>	203481	hum	2	10 µM	10									
204800	Aldosterone	203107	rat	2	10 µM	11									
205000	Anaphylatoxin C5a	203237	hum	2	10 µM	4									
205010	Androgen (Testosterone) AR	203102	rat	2	10 µM	4									
210020	Angiotensin AT <sub>1</sub>	203406	hum	2	10 µM	2									
210110	Angiotensin AT <sub>2</sub>	203095	hum	2	10 µM	4									
210700	APJ	203482	hum	2	10 µM	21									
211000	Atrial Natriuretic Factor (ANF)	203189	gp	2	10 µM	7									
211800	Bombesin B81	203483	hum	2	10 µM	3									
211700	Bombesin B82	203484	hum	2	10 µM	-3									
211800	Bombesin B83	203485	hum	2	10 µM	-2									
212510	Bradykinin B <sub>1</sub>	203086	hum	2	10 µM	5									
212610	Bradykinin B <sub>2</sub>	203087	hum	2	10 µM	3									
213810	Calcitonin	203238	hum	2	10 µM	-4									
214010	Calcitonin Gene-Related Peptide CGRP <sub>1</sub>	203239	hum	2	10 µM	15									
214510	Calcium Channel L-Type, Benzothiazepine	203056	rat	2	10 µM	27									
214800	Calcium Channel L-Type, Dihydropyridine	203057	rat	2	10 µM	-8									
215000	Calcium Channel L-Type, Phenylalkylamine	203058	rat	2	10 µM	28									

\* Batch: Represents compounds tested concurrently in the same assay(s). ‡ Partially soluble in *in vitro* test solvents.

‡ Denotes item meeting criteria for significance

† Results with ≥ 50% stimulation or inhibition are highlighted. (Negative values correspond to stimulation of binding or enzyme activity)

R=Additional Comments

gp=gulfus pig; hum=hamster; hum=human

PTW: 1094958  
CODE: AUS-122

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## EXPERIMENTAL RESULTS - BIOCHEMICAL ASSAYS

Cat. #	TARGET	BATCH*	SPC.	n=	CONC.	†% INHIBITION					IC <sub>50</sub>	K <sub>i</sub>	pH	R
						%	-100	-50	0	50	100			
216000	Calcium Channel N-Type	203176	rat	2	10 µM	0								
217020	Cannabinoid CB <sub>1</sub>	203177	hum	2	10 µM	14								
217100	Cannabinoid CB <sub>2</sub>	203178	hum	2	10 µM	-3								
244600	Chenokine CX3CR1	203471	hum	2	10 µM	24								
218010	Cholecystokinin CCK <sub>1</sub> (CCK <sub>A</sub> )	203408	hum	2	10 µM	21								
218120	Cholecystokinin CCK <sub>2</sub> (CCK <sub>B</sub> )	203468	hum	2	10 µM	-3								
219100	Colchicine	203000	rat	2	10 µM	-15								
219150	Corticotropin Releasing Factor CRF	203409	hum	2	10 µM	-6								
219500	Dopamine D <sub>1</sub>	202982	hum	2	10 µM	8								
219700	Dopamine D <sub>2</sub>	202984	hum	2	10 µM	3								
219800	Dopamine D <sub>3</sub>	202985	hum	2	10 µM	3								
219900	Dopamine D <sub>4</sub>	202986	hum	2	10 µM	7								
220200	Dopamine D <sub>5</sub>	202989	hum	2	10 µM	3								
224010	Endothelin ET <sub>A</sub>	203091	hum	2	10 µM	-14								
224110	Endothelin ET <sub>B</sub>	203092	hum	2	10 µM	14								
225510	Epidermal Growth Factor (EGF)	203167	hum	2	10 µM	4								
225800	Erythropoietin EPOR	203467	hum	2	10 µM	9								
• 226010	Estrogen ERα	202976	hum	2	10 µM	93								
• 226050	Estrogen ERβ	202977	hum	2	10 µM	94								
226300	G Protein-Coupled Receptor GPR103	202993	hum	2	10 µM	14								
226230	G Protein-Coupled Receptor GPR8	203470	hum	2	10 µM	0								
226610	GABA <sub>A</sub> Chloride Channel, TB08	203101	rat	2	10 µM	-1								
226680	GABA <sub>A</sub> , Flunitrazepam, Central	203081	rat	2	10 µM	5								
226500	GABA <sub>A</sub> , Muscimol, Central	203080	rat	2	10 µM	-8								
226610	GABA <sub>A</sub> α	203158	hum	2	10 µM	-6								
226710	GABA <sub>A</sub> β	203159	hum	2	10 µM	2								
230000	Gabapentin	203001	rat	2	10 µM	-12								
231510	Galanin GAL1	203165	hum	2	10 µM	-1								
231600	Galanin GAL2	203166	hum	2	10 µM	-6								
232800	Glutamate, AMPA	203157	rat	2	10 µM	1								

\* Batch: Represents compounds tested concurrently in the same assay(s). ‡ Partially soluble in *in vitro* test solvent.

• Denotes item meeting criteria for significance

† Results with ≥ 50% stimulation or inhibition are highlighted. (Negative values correspond to stimulation of binding or enzyme activity)

R=Additional Comments

gp=guinea pig; hem=hamster; hum=human

PT# 1094968  
CODE: A08-133

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## EXPERIMENTAL RESULTS - BIOCHEMICAL ASSAYS

Cat.#	TARGET	BATCH*	SPP.	n=	CONC.	↑% INHIBITION					IC <sub>50</sub>	K <sub>i</sub>	n <sub>H</sub>	R
						%	100	50	0	50	100			
232700	Glutamate, Kainate	203063	rat	2	10 µM	24								
232810	Glutamate, NMDA, Agonism	203064	rat	2	10 µM	23								
232810	Glutamate, NMDA, Glycine	203065	rat	2	10 µM	-4								
233000	Glutamate, NMDA, Phencyclidine	203068	rat	2	10 µM	-6								
234000	Glutamate, NMDA, Polyamine	203067	rat	2	10 µM	-1								
239000	Glycine, Strychnine-Sensitive	203068	rat	2	10 µM	-2								
239300	Growth Hormone Secretagogue (GHS, Ghrelin)	203243	hum	2	10 µM	0								
239810	Histamine H <sub>1</sub>	202870	hum	2	10 µM	5								
239710	Histamine H <sub>2</sub>	203069	hum	2	10 µM	15								
239810	Histamine H <sub>3</sub>	202872	hum	2	10 µM	5								
239900	Histamine H <sub>4</sub>	202873	hum	2	10 µM	-1								
241000	Imidazoline I <sub>2</sub> , Central	202874	rat	2	10 µM	-6								
242600	Inositol Trisphosphate IP <sub>3</sub>	203244	rat	2	10 µM	16								
243000	Insulin	203208	rat	2	10 µM	-2								
250400	Leptin	203317	mouse	2	10 µM	12								
250510	Leukotriene, BLT (LTB <sub>2</sub> )	203353	hum	2	10 µM	-5								
250480	Leukotriene, Cysteinyl CysLT <sub>1</sub>	203069	hum	2	10 µM	-18								
250480	Leukotriene, Cysteinyl CysLT <sub>2</sub>	203069	hum	2	10 µM	0								
251100	Melanocortin MC <sub>1</sub>	203411	hum	2	10 µM	7								
251300	Melanocortin MC <sub>2</sub>	203412	hum	2	10 µM	-1								
251350	Melanocortin MC <sub>3</sub>	203413	hum	2	10 µM	6								
251400	Melanocortin MC <sub>4</sub>	203414	hum	2	10 µM	10								
251600	Melatonin MT <sub>1</sub>	203140	hum	2	10 µM	1								
251700	Melatonin MT <sub>2</sub>	203142	hum	2	10 µM	33								
252200	Modlin	203472	hum	2	10 µM	14								
252810	Muscarinic M <sub>1</sub>	202957	hum	2	10 µM	-2								
252710	Muscarinic M <sub>2</sub>	202958	hum	2	10 µM	-5								
252810	Muscarinic M <sub>3</sub>	202959	hum	2	10 µM	0								
252910	Muscarinic M <sub>4</sub>	202980	hum	2	10 µM	3								
253010	Muscarinic M <sub>5</sub>	202981	hum	2	10 µM	2								
226100	N-Termyl Peptide Receptor FPR1	203240	hum	2	10 µM	-3								

\* Batch: Represents compounds tested concurrently in the same assay(s). ‡ Partially soluble in *in vitro* test solvent.

• Denotes term meeting criteria for significance

† Results with ≥ 50% stimulation or inhibition are highlighted. (Negative values correspond to stimulation of binding or enzyme activity)

R=Additional Comments

gp=guinea pig; ham=hamster; hum=human

## EXPERIMENTAL RESULTS - BIOCHEMICAL ASSAYS

Cat. #	TARGET	BATCH*	SPP.	Dose	CONC.	†% INHIBITION					IC <sub>50</sub>	K <sub>i</sub>	n <sub>H</sub>	R
						%	-100	-50	0	50	100			
226200	N-Fornyl Peptide Receptor-Like FPR1	203241	hum	2	10 µM	-12								
256100	Neuromedin U NMU <sub>1</sub>	203473	hum	2	10 µM	9								
256200	Neuromedin U NMU <sub>2</sub>	203474	hum	2	10 µM	2								
257010	Neuropeptide Y Y <sub>1</sub>	203093	hum	2	10 µM	3								
257110	Neuropeptide Y Y <sub>2</sub>	203094	hum	2	10 µM	6								
258010	Neurotensin NT <sub>1</sub>	203318	hum	2	10 µM	-4								
258590	Nicotinic Acetylcholine	202989	hum	2	10 µM	-6								
258700	Nicotinic Acetylcholine α1, Bungarotoxin	202991	hum	2	10 µM	7								
258830	Nicotinic Acetylcholine α7, Bungarotoxin	202990	rat	2	10 µM	-7								
280110	Opiate δ (OP1, DOP)	203070	hum	2	10 µM	0								
280210	Opiate κ (OP2, KOP)	203072	hum	2	10 µM	11								
280410	Opiate μ (OP3, MOP)	203074	hum	2	10 µM	-4								
280690	Orphanin ORL <sub>1</sub>	203476	hum	2	10 µM	4								
284500	Phorbol Ester	203076	mouse	2	10 µM	-8								
285010	Platelet Activating Factor (PAF)	203007	hum	2	10 µM	12								
286200	Platelet-Derived Growth Factor (PDGF)	202979	mouse	2	10 µM	0								
286500	Potassium Channel [K <sub>v</sub> ]	203079	rat	2	10 µM	0								
286600	Potassium Channel [K <sub>ir</sub> ]	203078	ham	2	10 µM	-12								
286800	Potassium Channel [SK <sub>Ca</sub> ]	203002	rat	2	10 µM	3								
286900	Potassium Channel HERG	202894	hum	2	10 µM	-18								
288020	Progesterone PR-B	202892	hum	2	10 µM	17								
288030	Prostanoid CRTH2	203352	hum	2	10 µM	-8								
288050	Prostanoid DP	202896	hum	2	10 µM	21								
288200	Prostanoid EP <sub>1</sub>	202898	hum	2	10 µM	19								
288410	Prostanoid EP <sub>2</sub>	202897	hum	2	10 µM	0								
288510	Prostanoid, Thromboxane A <sub>2</sub> (TP)	203271	hum	2	10 µM	-15								
288700	Purineric P <sub>2u</sub>	202982	rabbit	2	10 µM	15								
288810	Purineric P <sub>2v</sub>	202983	rat	2	10 µM	7								
289300	Rethoid X Receptor RORα	203477	hum	2	10 µM	3								

\* Batch: Represents compounds tested concurrently in the same assay(s). ‡ Partially soluble in *in vitro* test solvent.

• Denotes item meeting criteria for significance

† Results with ≥ 50% stimulation or inhibition are highlighted. (Negative values correspond to stimulation of binding or enzyme activity)

R=Additional Comments

gp=guinea pig; ham=hamster; hum=human

## EXPERIMENTAL RESULTS - BIOCHEMICAL ASSAYS

Cat. #	TARGET	BATCH*	SPP.	n=	CONC.	↑% INHIBITION					IC <sub>50</sub>	K <sub>i</sub>	Th <sub>1/2</sub>	R
						%	-100	-50	0	50	100			
270000	Rolipram	203130	rat	2	10 µM	2	↓	↓	↓	↓	↓			
270900	Ryanodine RyR3	203478	rat	2	10 µM	4	↓	↓	↓	↓	↓			
271110	Serotonin (5-Hydroxytryptamine) 5-HT <sub>1A</sub>	203108	hum	2	10 µM	-8			↓	↓	↓			
271200	Serotonin (5-Hydroxytryptamine) 5-HT <sub>1B</sub>	203109	rat	2	10 µM	18			↓	↓	↓			
271700	Serotonin (5-Hydroxytryptamine) 5-HT <sub>2A</sub>	203251	hum	2	10 µM	10			↓	↓	↓			
271800	Serotonin (5-Hydroxytryptamine) 5-HT <sub>2C</sub>	203273	hum	2	10 µM	13			↓	↓	↓			
271910	Serotonin (5-Hydroxytryptamine) 5-HT <sub>2</sub>	203184	hum	2	10 µM	-5			↓	↓	↓			
272000	Serotonin (5-Hydroxytryptamine) 5-HT <sub>6</sub>	203174	gp	2	10 µM	10			↓	↓	↓			
272100	Serotonin (5-Hydroxytryptamine) 5-HT <sub>1A</sub>	203003	hum	2	10 µM	4			↓	↓	↓			
272200	Serotonin (5-Hydroxytryptamine) 5-HT <sub>1</sub>	203254	hum	2	10 µM	28			↓	↓	↓			
276110	Sigma σ <sub>1</sub>	203082	hum	2	10 µM	7			↓	↓	↓			
276200	Sigma σ <sub>2</sub>	203083	rat	2	10 µM	14			↓	↓	↓			
279510	Sodium Channel, Site 2	203084	rat	2	10 µM	11			↓	↓	↓			
282510	Somatostatin sst1	203181	hum	2	10 µM	6			↓	↓	↓			
282700	Somatostatin sst2	203182	hum	2	10 µM	3			↓	↓	↓			
282830	Somatostatin sst3	203183	hum	2	10 µM	15			↓	↓	↓			
282900	Somatostatin sst4	203184	hum	2	10 µM	-1			↓	↓	↓			
283000	Somatostatin sst5	203185	hum	2	10 µM	-13			↓	↓	↓			
255810	Tachykinin NK <sub>1</sub>	203180	hum	2	10 µM	2			↓	↓	↓			
255860	Tachykinin NK <sub>2</sub>	203181	hum	2	10 µM	17			↓	↓	↓			
255710	Tachykinin NK <sub>3</sub>	203182	hum	2	10 µM	1			↓	↓	↓			
286800	Thyroid Hormone	203171	rat	2	10 µM	14			↓	↓	↓			
286900	Thyrotropin Releasing Hormone (TRH)	203259	rat	2	10 µM	-15			↓	↓	↓			
288200	Transforming Growth Factor-β (TGF-β)	202880	mouse	2	10 µM	10			↓	↓	↓			
202000	Transporter, Adenosine	203088	gp	2	10 µM	7			↓	↓	↓			
219000	Transporter, Choline	203105	rat	2	10 µM	17			↓	↓	↓			

\* Batch: Represents compounds tested concurrently in the same assay(s). ‡ Partially soluble in *in vitro* test solvent.

• Denotes item meeting criteria for significance

† Results with ≥ 50% stimulation or inhibition are highlighted. (Negative values correspond to stimulation of binding or enzyme activity)

Re: Additional Comments

gp=guinea pig; ham=hamster; hum=human

## EXPERIMENTAL RESULTS - BIOCHEMICAL ASSAYS

Cat. #	TARGET	BATCH*	SPP:	n=	CONC.	†% INHIBITION					IC <sub>50</sub>	K <sub>i</sub>	n <sub>H</sub>	R
						%	-100	-50	0	50	100			
‡ 226320	Transporter, Dopamine (DAT)	203168	hum	2	10 µM	88								
226400	Transporter, GABA	203059	rat	2	10 µM	6								
‡ 253010	Transporter, Monoamine	203425	rabbit	2	10 µM	51								
204410	Transporter, Norepinephrine (NET)	203054	hum	2	10 µM	37								
274030	Transporter, Serotonin (5-Hydroxytryptamine) (SERT)	203055	hum	2	10 µM	17								
286700	Urotensin II	203234	hum	2	10 µM	-15								
286810	Vanilloid	203193	rat	2	10 µM	-9								
286800	Vascular Endothelial Growth Factor (VEGF)	203041	hum	2	10 µM	6								
287010	Vasoactive Intestinal Peptide VIP <sub>1</sub>	203280	hum	2	10 µM	-9								
287620	Vasopressin V <sub>1A</sub>	203097	hum	2	10 µM	2								
287660	Vasopressin V <sub>1B</sub>	203088	hum	2	10 µM	-11								
287610	Vasopressin V <sub>2</sub>	203089	hum	2	10 µM	-18								
288000	Vitamin D <sub>3</sub>	203098	hum	2	10 µM	-1								

\* Batch: Represents compounds tested concurrently in the same assay(s). ‡ Partially soluble in *in vitro* test solvent.

‡ Denotes here meeting criteria for significance

† Results with ≥ 50% stimulation or inhibition are highlighted. (Negative values correspond to stimulation of binding or enzyme activity)

R-Additional Comments

gp=guinea pig; ham=hamster; hum=human

Job: 1094963  
CODE: AUS-111

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## EXPERIMENTAL RESULTS - BIOCHEMICAL ASSAYS

MDS has an exclusive, worldwide limited use license from Synaptic Pharmaceutical Corporation to perform these assays: Adrenergic Alpha 1D, Adrenergic Alpha 2B, and Dopamine D5 for safety and selectivity profiling. MDS' license excludes performing those assays in connection with drug discovery or development activities where the principal therapeutic mechanism of action of the test compound involves selective binding to a licensed receptor. Customers may contact Synaptic directly if they believe they need a broader license.



**SpectrumScreen  
Data Report  
Ausio Pharmaceuticals LLC**

Study Completed: August 27, 2007

Report Printed: August 27, 2007

**MDSPS PT#: 1094969**

**Alt. Code 1: Batch: NW037/07**

**Alt. Code 2:**

**Alt. Code 3:**

**Sample(s): AUS-133**

**M.W.: 242.27**

**Objectives:**

To evaluate, in SpectrumScreen, the activity of test compound AUS-133 (PT# 1094969).



File: 1094969  
Code: AUS-133

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## MDS Pharma Services Pharmacology Data Report On Compound AUS-133 For Ausio Pharmaceuticals LLC

Work Order Number: 1-1028408-1      Services Being Reported: SpectrumScreen  
Alternative Work Order No:  
Purchase Order Number:      Total # of Assays: 159  
Compound Information:  
    Compound Code: AUS-133  
    Alternative Code 1: Batch: NW03707  
    Alternative Code 2:  
    Alternative Code 3:  
    MDSPS Internal #: 1094969  
    Molecular Weight: 242.27  
Sponsor: Ausio Pharmaceuticals LLC  
    1776 Mentor Avenue  
    Suite 340  
    Cincinnati, OH 45212  
    USA  
Undertaken at: MDS Pharma Services - Taiwan Ltd.  
    Pharmacology Laboratories  
    158 Li-Teh Road, Pailou  
    Taipai, Taiwan 112  
    Taiwan  
Date of Study: August 13, 2007 - August 27, 2007  
Study Directors: Kun-Yuan Lin, MDS Pharma Services - Taiwan Ltd.  
    Kuo-Hsin Chen, MDS Pharma Services - Taiwan Ltd.  
Distribution: Ausio Pharmaceuticals LLC

"This study was conducted according to the procedures described in this report. All data presented are authentic, accurate and correct to the best of our knowledge."

*Kun-Yuan Lin*

Kun-Yuan Lin  
Study Director for Animal Assays

*Kuo-Hsin Chen*

Kuo-Hsin Chen  
Study Director for Biochemical Assays

*Jian-Wu Wei*

Jian-Wu Wei, Ph.D  
Quality Control and Data Reviewer

*Peter Chiu*

Peter Chiu, Ph.D  
Technical Director

FILE: 10499  
CODE: A05-133

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## SUMMARY

### STUDY OBJECTIVE

To evaluate, in Radioligand Binding assays, the activity of compound AUS-133 (PT# 1094969).

### METHODS

Methods employed in this study have been adapted from the scientific literature to maximize reliability and reproducibility. Reference standards were run as an integral part of each assay to ensure the validity of the results obtained. Assays were performed under conditions described in the accompanying "Methods" section of this report. The literature reference(s) for each assay are in the "Literature References" section. If either of these sections were not originally requested with the accompanying report, please contact us at the number below for a printout of either of these report sections.

Where presented,  $IC_{50}$  values were determined by a non-linear, least squares regression analysis using Data Analysis Toolbox™ (MDL Information Systems, San Leandro, CA, USA). Where inhibition constants ( $K_i$ ) are presented, the  $K_i$  values were calculated using the equation of Cheng and Prusoff (Cheng, Y., Prusoff, W.H., *Biochem. Pharmacol.* 22:3099-3108, 1973) using the observed  $IC_{50}$  of the tested compound, the concentration of radioligand employed in the assay, and the historical values for the  $K_o$  of the ligand (obtained experimentally at MDS Pharma Services). Where presented, the Hill coefficient ( $n_H$ ), defining the slope of the competitive binding curve, was calculated using Data Analysis Toolbox™. Hill coefficients significantly different than 1.0, may suggest that the binding displacement does not follow the laws of mass action with a single binding site. Where  $IC_{50}$ ,  $K_i$  and/or  $n_H$  data are presented without Standard Error of the Mean (SEM), data are insufficient to be quantitative, and the values presented ( $K_i$ ,  $IC_{50}$ ,  $n_H$ ) should be interpreted with caution.

### RESULTS

A summary of results meeting the significance criteria is presented in the following sections. Complete results are presented under the section labeled "Experimental Results". Individual responses, if requested, are presented in the appendix to this report.

### SUMMARY/CONCLUSION

Significant results are displayed in the following table(s) in rank order of potency for estimated  $IC_{50}$  and/or  $K_i$  values.

## SUMMARY OF SIGNIFICANT PRIMARY RESULTS

Biochemical assay results are presented as the percent inhibition of specific binding or activity throughout the report. All other results are expressed in terms of that assay's quantitation method (see Methods section).

- For primary assays, only the lowest concentration with a significant response judged by the assays' criteria, is shown in this summary.
- Where applicable, either the secondary assay results with the lowest dose/concentration meeting the significance criteria or, if inactive, the highest dose/concentration that did not meet the significance criteria is shown.
- Unless otherwise requested, primary screening in duplicate with quantitative data (e.g.,  $IC_{50} \pm SEM$ ,  $K_i \pm SEM$  and  $nH$ ) are shown where applicable for individual requested assays. In screening packages, primary screening in duplicate with semi-quantitative data (e.g., estimated  $IC_{50}$ ,  $K_i$  and  $nH$ ) are shown where applicable (concentration range of 4 log units);\* available secondary functional assays are carried out (30  $\mu M$ ) and MEC or MIC determined only if active in primary assays >50% at 1 log unit below initial test concentration.
- Please see Experimental Results section for details of all responses.

Significant responses ( $\geq 50\%$  inhibition or stimulation for Biochemical assays) were noted in the primary assays listed below:

PRIMARY TESTS							
CAT. #	PRIMARY BIOCHEMICAL ASSAY	SPECIES	CONC.	% INH.	$IC_{50}$ *	$K_i$	$nH$
204410	Transporter, Norepinephrine (NET)	hum	10 $\mu M$	50			
220320	Transporter, Dopamine (DAT)	hum	10 $\mu M$	92			
226010	Estrogen ER $\alpha$	hum	10 $\mu M$	94			
226050	Estrogen ER $\beta$	hum	10 $\mu M$	98			

‡ Partially soluble in in vitro test solvent.

\* A standard error of the mean is presented where results are based on multiple, independent determinations.

gp=guinea pig; ham=hamster; hum=human

## EXPERIMENTAL RESULTS - BIOCHEMICAL ASSAYS

Cell	TARGET	BATCH*	SPP.	Dose	CONC.	↑% INHIBITION					IC <sub>50</sub>	K <sub>i</sub>	pH	R
						%	-100	-50	0	50	100			
200510	Adenosine A <sub>1</sub>	203049	hum	2	10 µM	-6								
200610	Adenosine A <sub>2A</sub>	203053	hum	2	10 µM	24								
200720	Adenosine A <sub>3</sub>	203104	hum	2	10 µM	15								
203100	Adrenergic α <sub>1A</sub>	203043	rat	2	10 µM	9								
203200	Adrenergic α <sub>1B</sub>	203044	rat	2	10 µM	2								
203400	Adrenergic α <sub>1D</sub>	203045	hum	2	10 µM	-8								
203820	Adrenergic α <sub>2A</sub>	203048	hum	2	10 µM	10								
203800	Adrenergic α <sub>2C</sub>	203048	hum	2	10 µM	5								
204010	Adrenergic β <sub>1</sub>	203050	hum	2	10 µM	8								
204110	Adrenergic β <sub>2</sub>	203051	hum	2	10 µM	8								
204200	Adrenergic β <sub>3</sub>	203052	hum	2	10 µM	-5								
204480	Adrenomedullin AM <sub>1</sub>	203460	hum	2	10 µM	-2								
204470	Adrenomedullin AM <sub>2</sub>	203461	hum	2	10 µM	9								
204800	Aldosterone	203107	rat	2	10 µM	20								
205000	Anaphylatoxin C5a	203237	hum	2	10 µM	-7								
205010	Androgen (Testosterone) AR	203102	rat	2	10 µM	5								
210020	Angiotensin AT <sub>1</sub>	203408	hum	2	10 µM	-14								
210110	Angiotensin AT <sub>2</sub>	203095	hum	2	10 µM	1								
210700	APJ	203482	hum	2	10 µM	-10								
211000	Atrial Natriuretic Factor (ANF)	203189	gp	2	10 µM	4								
211600	Bombesin BB1	203483	hum	2	10 µM	7								
211700	Bombesin BB2	203484	hum	2	10 µM	-1								
211800	Bombesin BB3	203485	hum	2	10 µM	-12								
212510	Bradykinin B <sub>1</sub>	203086	hum	2	10 µM	8								
212910	Bradykinin B <sub>2</sub>	203087	hum	2	10 µM	13								
213810	Calcitonin	203238	hum	2	10 µM	-1								
214010	Calcitonin Gene-Related Peptide CGRP <sub>1</sub>	203239	hum	2	10 µM	8								
214510	Calcium Channel L-Type, Benzothiadiazepine	203056	rat	2	10 µM	21								
214800	Calcium Channel L-Type, Dihydropyridine	203057	rat	2	10 µM	0								
215000	Calcium Channel L-Type, Phenylalkylamine	203058	rat	2	10 µM	38								

\* Batch: Represents compounds tested concurrently in the same assay(s). ‡ Partially soluble in *in vitro* test solvent.

† Denotes *in vitro* screening criteria for significance

‡ Results with ≥ 50% stimulation or inhibition are highlighted. (Negative values correspond to stimulation of binding or enzyme activity)

R=Additional Comments

gp=guinea pig; ham=hamster; hum=human

## EXPERIMENTAL RESULTS - BIOCHEMICAL ASSAYS

Cat. #	TARGET	BATCH*	SPP.	n=	CONC.	↑% INHIBITION					IC <sub>50</sub>	H <sub>0</sub>	H <sub>1</sub>	H <sub>2</sub>
						%	-100	-50	0	50	100			
216000	Calcium Channel N-Type	203178	rat	2	10 µM	-4								
217020	Cannabinoid CB <sub>1</sub>	203177	hum	2	10 µM	11								
217100	Cannabinoid CB <sub>2</sub>	203178	hum	2	10 µM	6								
244800	Chemokine CXCR1	203471	hum	2	10 µM	11								
218010	Cholecystokinin CCK <sub>1</sub> (CCK <sub>A</sub> )	203408	hum	2	10 µM	20								
218120	Cholecystokinin CCK <sub>2</sub> (CCK <sub>B</sub> )	203488	hum	2	10 µM	1								
219100	Colchicine	203000	rat	2	10 µM	22								
219150	Corticotropin Releasing Factor CRF <sub>1</sub>	203409	hum	2	10 µM	-3								
219500	Dopamine D <sub>1</sub>	202962	hum	2	10 µM	0								
219700	Dopamine D <sub>2</sub>	202984	hum	2	10 µM	-5								
219800	Dopamine D <sub>3</sub>	202985	hum	2	10 µM	-5								
219900	Dopamine D <sub>4</sub>	202986	hum	2	10 µM	11								
220200	Dopamine D <sub>5</sub>	202969	hum	2	10 µM	7								
224010	Endothelin ET <sub>A</sub>	203091	hum	2	10 µM	-5								
224110	Endothelin ET <sub>B</sub>	203092	hum	2	10 µM	2								
225510	Epidermal Growth Factor (EGF)	203187	hum	2	10 µM	-6								
225800	Erythropoietin EPOR	203883	hum	2	10 µM	3								
• 228010	Estrogen ERα	202976	hum	2	10 µM	94								
• 228050	Estrogen ERβ	202977	hum	2	10 µM	98								
228300	G Protein-Coupled Receptor GPR103	202983	hum	2	10 µM	98								
228230	G Protein-Coupled Receptor GPR8	203470	hum	2	10 µM	1								
228910	GABA <sub>A</sub> Chloride Channel, TBOB	203101	rat	2	10 µM	3								
228800	GABA <sub>A</sub> , Flunitrazepam, Central	203081	rat	2	10 µM	1								
228500	GABA <sub>A</sub> , Muscimol, Central	203080	rat	2	10 µM	-1								
228810	GABA <sub>A</sub> α1	203158	hum	2	10 µM	-1								
228710	GABA <sub>A</sub> α5	203158	hum	2	10 µM	-6								
230000	Gabapentin	203001	rat	2	10 µM	-17								
231510	Galanin GAL1	203165	hum	2	10 µM	-5								
231600	Galanin GAL2	203166	hum	2	10 µM	-3								
232800	Glutamate, AMPA	203157	rat	2	10 µM	-6								

\* Batch: Represents compounds tested concurrently in the same assay(s). ‡ Partially soluble in *in vitro* test solvent.

• Denotes item meeting criteria for significance

† Results with ≥ 50% stimulation or inhibition are highlighted. (Negative values correspond to stimulation of binding or enzyme activity)

R=Additional Comments

gp=guinea pig; hum=hamster; hum=human

## EXPERIMENTAL RESULTS - BIOCHEMICAL ASSAYS

Cat. #	TARGET	BATCH*	SPR	NO	CONC.	↑% INHIBITION					IC <sub>50</sub>	K <sub>i</sub>	T <sub>1/2</sub>	R
						%	-100	-50	0	50	100			
232700	Glutamate, Kainate	203063	rat	2	10 µM	18								
232810	Glutamate, NMDA, Agonism	203064	rat	2	10 µM	24								
232910	Glutamate, NMDA, Glycine	203065	rat	2	10 µM	-5								
233000	Glutamate, NMDA, Phencyclidine	203066	rat	2	10 µM	9								
234000	Glutamate, NMDA, Polyamine	203067	rat	2	10 µM	6								
239000	Glycine, Strychnine-Sensitive	203068	rat	2	10 µM	12								
239900	Growth Hormone Secretagogue (GHS, Ghrelin)	203243	hum	2	10 µM	12								
239810	Histamine H <sub>1</sub>	202870	hum	2	10 µM	11								
239710	Histamine H <sub>2</sub>	203069	hum	2	10 µM	7								
239810	Histamine H <sub>3</sub>	202872	hum	2	10 µM	18								
239900	Histamine H <sub>4</sub>	202873	hum	2	10 µM	-1								
241000	Imidazoline I <sub>2</sub> , Central	202874	rat	2	10 µM	-13								
242500	Inositol Trisphosphate IP <sub>3</sub>	203244	rat	2	10 µM	11								
243000	Insulin	203208	rat	2	10 µM	-2								
250400	Leptin	203317	mouse	2	10 µM	2								
250510	Leukotriene, BLT (LTB <sub>4</sub> )	203353	hum	2	10 µM	-25								
250480	Leukotriene, Cysteinyl CysLT <sub>1</sub>	203089	hum	2	10 µM	3								
250480	Leukotriene, Cysteinyl CysLT <sub>2</sub>	203090	hum	2	10 µM	-49								
251100	Melanocortin MC <sub>1</sub>	203411	hum	2	10 µM	1								
251300	Melanocortin MC <sub>3</sub>	203412	hum	2	10 µM	-5								
251350	Melanocortin MC <sub>4</sub>	203413	hum	2	10 µM	3								
251400	Melanocortin MC <sub>5</sub>	203414	hum	2	10 µM	8								
251600	Melatonin MT <sub>1</sub>	203140	hum	2	10 µM	14								
251700	Melatonin MT <sub>2</sub>	203142	hum	2	10 µM	48								
252200	Moulin	203472	hum	2	10 µM	-1								
252610	Muscarinic M <sub>1</sub>	202857	hum	2	10 µM	3								
252710	Muscarinic M <sub>2</sub>	202858	hum	2	10 µM	-4								
252810	Muscarinic M <sub>3</sub>	202859	hum	2	10 µM	0								
252810	Muscarinic M <sub>4</sub>	202860	hum	2	10 µM	8								
258010	Muscarinic M <sub>5</sub>	202861	hum	2	10 µM	-1								
228100	N-Formyl Peptide Receptor (FPR)	203240	hum	2	10 µM	-6								

\* Batch: Represents compounds tested concurrently in the same assay(s). † Partially soluble in *in vitro* test solvent.

• Denotes non meeting criteria for significance

† Results with ≥ 50% stimulation or inhibition are highlighted. (Negative values correspond to stimulation of binding or enzyme activity)

R=Additional Comments

gp=guinea pig; ham=hamster; hum=human



## EXPERIMENTAL RESULTS - BIOCHEMICAL ASSAYS

Cat. #	TARGET	BATCH*	SPP.	n	CONC.	†% INHIBITION					EC <sub>50</sub>	K <sub>i</sub>	n <sub>H</sub>	R
						%	-100	-50	0	50	100			
228200	N-Formyl Peptide Receptor-Like FFR1	203241	hum	2	10 µM	-7								
256100	Neurokinin U NMR <sub>1</sub>	203473	hum	2	10 µM	8								
256200	Neurokinin U NMR <sub>2</sub>	203474	hum	2	10 µM	-5								
257010	Neuropeptide Y Y <sub>1</sub>	203089	hum	2	10 µM	7								
257110	Neuropeptide Y Y <sub>2</sub>	203084	hum	2	10 µM	6								
258010	Neurotensin NT <sub>1</sub>	203318	hum	2	10 µM	-9								
258590	Nicotinic Acetylcholine	202889	hum	2	10 µM	-6								
258700	Nicotinic Acetylcholine α1, Bungarotoxin	202891	hum	2	10 µM	12								
258830	Nicotinic Acetylcholine α7, Bungarotoxin	202890	rat	2	10 µM	2								
260110	Opiate δ (OP1, DOP)	203070	hum	2	10 µM	12								
260210	Opiate κ (OP2, KOP)	203072	hum	2	10 µM	16								
260410	Opiate μ (OP3, MOP)	203074	hum	2	10 µM	-9								
260800	Orphanin ORL <sub>1</sub>	203476	hum	2	10 µM	7								
264500	Phorbol Ester	203078	mouse	2	10 µM	-8								
265010	Platelet Activating Factor (PAF)	203007	hum	2	10 µM	9								
265200	Platelet-Derived Growth Factor (PDGF)	202979	mouse	2	10 µM	9								
265500	Potassium Channel [K <sub>v</sub> ]	203079	rat	2	10 µM	-1								
265600	Potassium Channel [K <sub>cs</sub> ]	203078	ham	2	10 µM	-6								
265800	Potassium Channel [SK <sub>ca</sub> ]	203002	rat	2	10 µM	2								
265900	Potassium Channel HERG	202994	hum	2	10 µM	6								
268020	Progesterone PR-B	202992	hum	2	10 µM	15								
268030	Prostanoid CRTH2	203352	hum	2	10 µM	3								
268050	Prostanoid DP	202995	hum	2	10 µM	29								
268200	Prostanoid EP <sub>2</sub>	202996	hum	2	10 µM	14								
268410	Prostanoid EP <sub>4</sub>	202997	hum	2	10 µM	7								
268510	Prostanoid, Thromboxane A <sub>2</sub> (TP)	203004	hum	2	10 µM	-7								
268700	Purinergic P <sub>2U</sub>	203308	rabbit	2	10 µM	8								
268810	Purinergic P <sub>2Y</sub>	202983	rat	2	10 µM	3								
269500	Retinoid X Receptor RXRα	203477	hum	2	10 µM	-2								

\* Batch: Represents compounds tested concurrently in the same assay(s). ‡ Partially soluble in *in vitro* test solvent.

† Denotes items meeting criteria for significance

‡ Results with ≥ 50% stimulation or inhibition are highlighted. (Negative values correspond to stimulation of binding or enzyme activity)

R=Additional Comments

g=g Guinea pig; ham=hamster; hum=human

## EXPERIMENTAL RESULTS - BIOCHEMICAL ASSAYS

Cat. #	TARGET	BATCH*	SPP.	DO	CONC.	†% INHIBITION					IC <sub>50</sub>	K <sub>i</sub>	R <sub>0</sub>	R
						%	-100	-50	0	50	100			
270000	Rolipram	203130	rat	2	10 µM	13								
270300	Ryanodine RYR3	203478	rat	2	10 µM	4								
271110	Serotonin (5-hydroxytryptamine) 5-HT <sub>1A</sub>	203108	hum	2	10 µM	2								
271200	Serotonin (5-hydroxytryptamine) 5-HT <sub>1B</sub>	203109	rat	2	10 µM	19								
271700	Serotonin (5-hydroxytryptamine) 5-HT <sub>2A</sub>	203251	hum	2	10 µM	25								
271800	Serotonin (5-hydroxytryptamine) 5-HT <sub>2C</sub>	203273	hum	2	10 µM	9								
271910	Serotonin (5-hydroxytryptamine) 5-HT <sub>2B</sub>	203184	hum	2	10 µM	0								
272000	Serotonin (5-hydroxytryptamine) 5-HT <sub>4</sub>	203174	gp	2	10 µM	9								
272100	Serotonin (5-hydroxytryptamine) 5-HT <sub>6A</sub>	203003	hum	2	10 µM	3								
272200	Serotonin (5-hydroxytryptamine) 5-HT <sub>6B</sub>	203254	hum	2	10 µM	27								
278110	Sigma α <sub>1</sub>	203092	hum	2	10 µM	1								
278200	Sigma α <sub>2</sub>	203093	rat	2	10 µM	18								
278510	Sodium Channel, Site 2	203084	rat	2	10 µM	12								
282510	Somatostatin sst1	203181	hum	2	10 µM	6								
282710	Somatostatin sst2	203182	hum	2	10 µM	-11								
282810	Somatostatin sst3	203183	hum	2	10 µM	0								
282900	Somatostatin sst4	203184	hum	2	10 µM	12								
283000	Somatostatin sst5	203185	hum	2	10 µM	-11								
285510	Tachykinin NK <sub>1</sub>	203160	hum	2	10 µM	10								
285600	Tachykinin NK <sub>2</sub>	203161	hum	2	10 µM	22								
285710	Tachykinin NK <sub>3</sub>	203162	hum	2	10 µM	0								
285800	Thyroid Hormone	203171	rat	2	10 µM	0								
286110	Thyrotropin Releasing Hormone (TRH)	203259	rat	2	10 µM	1								
286210	Transforming Growth Factor-β (TGF-β)	202980	mouse	2	10 µM	8								
202000	Transporter, Adenosine	203088	gp	2	10 µM	6								
219000	Transporter, Choline	203105	rat	2	10 µM	-13								

\* Batch: Represents compounds tested concurrently in the same assay(s). ‡ Partially soluble in *in vitro* test solvent.

• Do: does not meet criteria for significance

† Results with ≥ 50% stimulation or inhibition are highlighted. (Negative values correspond to stimulation of binding or enzyme activity)

R=Assay Comments

gp=guinea pig; ham=hamster; hum=human

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## EXPERIMENTAL RESULTS - BIOCHEMICAL ASSAYS

Cat. #	TARGET	BATCH*	SPP.	no	CONC.	↑% INHIBITION					IC <sub>50</sub>	K <sub>i</sub>	n <sub>H</sub>	R
						%	-125	-50	0	50	100			
220370	Transporter, Dopamine (DAT)	203188	hum	2	10 µM	82								
225400	Transporter, GABA	203287	rat	2	10 µM	12								
252010	Transporter, Monoamine	203179	rabbi	2	10 µM	48								
204410	Transporter, Norepinephrine (NET)	203064	hum	2	10 µM	50								
274030	Transporter, Serotonin (5-Hydroxytryptamine) (SERT)	203055	hum	2	10 µM	15								
286700	Urotensin II	203234	hum	2	10 µM	-16								
288810	Vanilloid	203133	rat	2	10 µM	-3								
286970	Vascular Endothelial Growth Factor (VEGF)	203041	hum	2	10 µM	-3								
287010	Vasoactive Intestinal Peptide VIP <sub>1</sub>	203260	hum	2	10 µM	-1								
287570	Vasopressin V <sub>1A</sub>	203087	hum	2	10 µM	-1								
287560	Vasopressin V <sub>1B</sub>	203088	hum	2	10 µM	-14								
287810	Vasopressin V <sub>2</sub>	203099	hum	2	10 µM	-19								
288070	Vitamin D <sub>3</sub>	203098	hum	2	10 µM	-9								

\* Batch: Represents compounds tested concurrently in the same assay(s). ‡ Partially soluble in *in vitro* test solvent.

• Denotes item meeting criteria for significance

† Results with ≥ 50% stimulation or inhibition are highlighted. (Negative values correspond to stimulation of binding or enzyme activity)

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## EXPERIMENTAL RESULTS - BIOCHEMICAL ASSAYS

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